Biotechnology

Third edition

John E. Smith
Professor of Applied Microbiology, Strathclyde University

Published in association with the Institute of Biology

CAMBRIDGE
UNIVERSITY PRESS

PUBLISHED BY THE PRESS SYNDICATE OF THE UNIVERSITY OF CAMBRIDGE
The Pitt Building, Trumpington Street, Cambridge, United Kingdom

CAMBRIDGE UNIVERSITY PRESS
The Edinburgh Building, Cambridge CB2 2RU, UK
40 West 20th Street, New York, NY 10011-4211, USA
477 Williamstown Road, Port Melbourne, VIC 3207, Australia
Ruiz de Alarcón 13, 28014 Madrid, Spain
Dock House, The Waterfront, Cape Town 8001, South Africa

http://www.cambridge. org

First edition published by Edward Arnold 1981 (0 7131 2960 3)
Second edition 1988
Third edition first published by Cambridge University Press 1996
Third edition reprinted 1997, 1998, 2000, 2001, 2002

Printed in the United Kingdom at the University Press, Cambridge

Typeset in Monotype Garamond 11/13pt [SE]

A catalogue record for this book is available from the British Library

Library of Congress Cataloguing in Publication data
Smith, John E.
Biotechnology / John E. Smith. – 3rd ed.
p. cm.
Includes bibliographical references and index.
ISBN 0 521 44467 5 (hc). – ISBN 0 521 44911 1 (pb)
1. Biotechnology. I. Title.
TP248.2.S66 1996
660.6–dc20 95-35167 CIP

ISBN 0 521 44467 5 hardback
ISBN 0 521 44911 1 paperback

Contents

1

An introduction to biotechnology

1.1 What is biotechnology?

There is little doubt that modern biology is the most diversified of all the natural sciences, exhibiting a bewildering array of subdisciplines: microbiology, plant and animal anatomy, biochemistry, immunology, cell biology, molecular biology, plant and animal physiology, morphogenesis, systematics, ecology, genetics and many others. The increasing diversity of modern biology has been derived primarily from the largely post-war introduction into biology of other scientific disciplines such as physics, chemistry and mathematics, which has made possible the description of life processes at the cellular and molecular level. In the last two decades well over 20 Nobel prizes have been awarded for discoveries in these fields of study.

This newly acquired biological knowledge has already made vastly important contributions to the health and welfare of humankind. Yet few people fully recognise that the life sciences affect over 30% of global economic turnover by way of healthcare, food and energy, agriculture and forestry, and that this economic impact will grow as biotechnology provides new ways of influencing raw material processing. Biotechnology will increasingly affect the efficiency of all fields involving the life sciences and it is now realistically accepted that by the early twenty-first century, it will be contributing many trillions of dollars to world markets.

In the following chapters, biotechnology will be shown to cover a multitude of different applications ranging from the very simple and traditional, such as the production of beers, wines and cheeses, to highly complex molecular processes, such as the use of recombinant DNA technologies to yield new

Table 1.1. *Some selected definitions of biotechnology*

The application of biological organisms, systems or processes to manufacturing and service industries
The integrated use of biochemistry, microbiology and engineering sciences in order to achieve technological (industrial) application capabilities of microorganisms, cultured tissue cells and parts thereof
A technology using biological phenomena for copying and manufacturing various kinds of useful substance
The application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services
The science of the production processes based on the action of microorganisms and their active components and of production processes involving the use of cells and tissues from higher organisms. Medical technology, agriculture and traditional crop breeding are not generally regarded as biotechnology
Biotechnology is really no more than a name given to a set of techniques and processes
Biotechnology is the use of living organisms and their components in agriculture, food and other industrial processes
Biotechnology – the deciphering and use of biological knowledge

drugs or to introduce new traits into commercial crops and animals. The association of traditional industries such as brewing with modern genetic engineering is gaining momentum and it is not for nothing that industrial giants such as Guinness, Carlsberg and Bass are heavily involved in biotechnology research. Biotechnology is developing at a phenomenal pace and will increasingly be seen as a necessary part of the advance of modern life and not simply a way to make money!

While biotechnology has been defined in many forms (Table 1.1), in essence it implies the use of microbial, animal or plant cells or enzymes to synthesise, breakdown or transform materials.

The European Federation of Biotechnology (EFB) considers biotechnology as 'the integration of natural sciences and organisms, cells, parts thereof, and molecular analogues for products and services'. The aims of this Federation are:

(1) To advance biotechnology for the public benefit.
(2) To promote awareness, communication and collaboration in all fields of biotechnology.

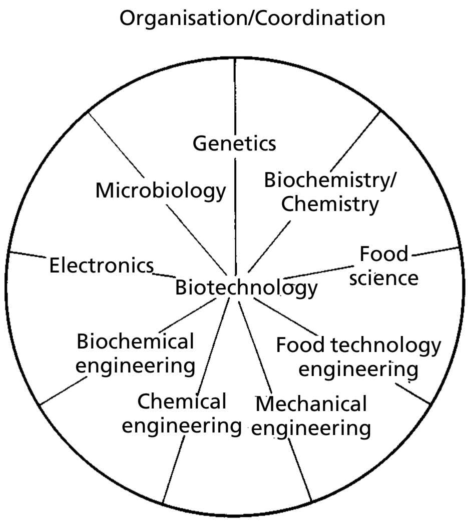

Fig. 1.1 The interdisciplinary nature of biotechnology (from Higgins *et al.*, 1985).

(3) To provide governmental and supranational bodies with information and informed opinions on biotechnology.
(4) To promote public understanding of biotechnology.

The EFB definition is applicable to both 'traditional or old' and 'new or modern' biotechnology. Traditional biotechnology refers to the conventional techniques that have been used for many centuries to produce beer, wine, cheese and many other foods, while 'new' biotechnology embraces all methods of genetic modification by recombinant DNA and cell fusion techniques, together with the modern developments of 'traditional' biotechnological processes. The difficulties of defining biotechnology and the resulting misunderstandings have led some people to suggest the abandonment of the term 'biotechnology' as too general and to replace it by the precise term of whatever specific technology or application was being used.

Unlike a single scientific discipline, biotechnology can draw upon a wide array of relevant fields such as microbiology, biochemistry, molecular biology, cell biology, immunology, protein engineering, enzymology, classified breeding techniques, and the full range of bioprocess technologies (Fig. 1.1). Biotechnology is not itself a product or range of products like microelectronics: rather it should be regarded as a range of enabling technologies that will find significant application in many industrial sectors. As will be seen in later

Table 1.2. *Historical development of biotechnology*

Biotechnological production of foods and beverages Sumarians and Babylonians were drinking beer by 6000 B.C.; Egyptians were baking leavened bread by 4000 B.C.; wine was known in the Near East by the time the book of Genesis was written. Microorganisms first seen in seventeenth century by Antonie van Leeuwenhoek, who developed the simple microscope; fermentative ability of microorganisms demonstrated between 1857 and 1876 by Pasteur – the father of biotechnology; cheese production has ancient origins; so also has mushroom cultivation
Biotechnological processes initially developed under non-sterile conditions Ethanol, acetic acid, butanol and acetone were produced by the end of the nineteenth century by open microbial fermentation processes; waste-water treatment and municipal composting of solid wastes were the largest fermentation capacity practised throughout the world
Introduction of sterility to biotechnological processes In the 1940s complicated engineering techniques were introduced to the mass cultivation of microorganisms to exclude contaminating microorganisms. Examples include antibiotics, amino acids, organic acids, enzymes, steroids, polysaccharides, vaccines and monoclonal antibodies
Applied genetics and recombinant DNA technology Traditional strain improvement of important industrial organisms has long been practised; recombinant DNA techniques together with protoplast fusion allow new programming of the biological properties of organisms

sections, it is a technology in search of new applications and the main benefits lie in the future. New biotechnological processes will, in many instances, function at low temperature, will consume little energy and will rely mainly on inexpensive substrates for biosynthesis.

However, it should be recognised that biotechnology is not something new but represents a developing and expanding series of technologies dating back (in many cases) thousands of years, to when humans first began unwittingly to use microbes to produce foods and beverages such as bread and beer and to modify plants and animals through progressive selection for desired traits. Biotechnology encompasses many traditional processes such as brewing, baking, wine-making, cheese production, the production of oriental foods such as soy sauce and tempeh, and sewage treatment where the use of microorganisms has been developed somewhat empirically over countless years (Table 1.2). It is only relatively recently that these processes have been subjected to rigorous scientific scrutiny and analysis; even so it will surely take some time for modern scientifically based practices fully to replace traditional empiricism.

The new biotechnology revolution began in the 1970s and early 1980s, when scientists learned to alter precisely the genetic constitution of living organisms by processes outwith traditional breeding practices. This 'genetic engineering' has had a profound impact on almost all areas of traditional biotechnology and further permitted breakthroughs in medicine and agriculture, in particular those that would be impossible by traditional breeding approaches. Some of the most exciting advances will be in new pharmaceutical drugs and gene therapies to treat previously incurable diseases, to produce healthier foods, safer pesticides, innovative environmental technologies and new energy sources.

There is also a considerable danger that biotechnology will be viewed as a coherent, unified body of scientific and engineering knowledge and thinking to be applied in a coherent and logical manner. This is not so: the range of biological, chemical and engineering disciplines that is involved is having varying degrees of application to the industrial scene.

Traditional biotechnology has established a huge and expanding world market and, in monetary terms, represents a major part of *all* biotechnology financial profits. 'New' aspects of biotechnology founded in recent advances in molecular biology, genetic engineering and fermentation process technology are now increasingly finding wide industrial application. A breadth of relevant biological and engineering knowledge and expertise is ready to be put to productive use; but the rate that it will be applied will depend less on scientific or technical considerations and more on such factors as adequate investment by the relevant industries, improved systems of biological patenting, marketing skills, the economics of the new methods in relation to current technologies and, possibly of most importance, public perception and acceptance.

The industrial activities to be affected will include human and animal food production, provision of chemical feedstocks to replace petrochemical sources, alternative energy sources, waste recycling, pollution control, agriculture and forestry. The new techniques will also revolutionise many aspects of medicine, veterinary sciences, and pharmaceutics.

Biotechnological industries will be based largely on renewable and recyclable materials and so can be adapted to the needs of a society in which energy is ever increasingly expensive and scarce. In many ways, biotechnology is a series of embryonic technologies and will require much skilful control of its development, but the potentials are vast and diverse, and undoubtedly will play an increasingly important part in many future industrial processes.

1.2 Biotechnology – an interdisciplinary pursuit

Biotechnology is *a priori* an interdisciplinary pursuit. In recent decades a characteristic feature of the development of science and technology has been the increasing resort to multidisciplinary strategies for the solution of various problems. This has led to the emergence of new interdisciplinary areas of study, with the eventual crystallisation of new disciplines with identifiable characteristic concepts and methodologies. Chemical engineering and biochemistry are two well-recognised examples of disciplines that have done much to clarify our understanding of chemical processes and the biochemical bases of biological systems.

The term 'multidisciplinary' describes a quantitative extension of approaches to problems that commonly occur within a given area. It involves the marshalling of concepts and methodologies from a number of separate disciplines and applying them to a specific problem in another area. In contrast, interdisciplinary application occurs when the blending of ideas that occur during multidisciplinary cooperation leads to the crystallisation of a new disciplinary area with its own concepts and methodologies. In practice, multidisciplinary enterprises are almost invariably mission orientated. However, when true interdisciplinary synthesis occurs the new area will open up a novel spectrum of investigations. Many aspects of biotechnology have arisen through the interaction between various parts of biology and engineering.

A biotechnologist can utilise techniques derived from chemistry, microbiology, biochemistry, chemical engineering and computer science (Fig. 1.1). The main objectives will be the innovation, development and optimal operation of processes in which biochemical catalysis has a fundamental and irreplaceable role. Biotechnologists must also aim to achieve a close working cooperation with experts from other related fields such as medicine, nutrition, the pharmaceutical and chemical industries, environmental protection and waste process technology. The application of biotechnology will increasingly rely upon each of the contributing disciplines for an understanding of the technical language of the others and, above all, an understanding of the potential as well as the limitations of the other areas.

Biotechnology is a demanding industry that requires a skilled workforce and a supportive public to ensure continued growth. Economies that encourage public understanding and provide a competent labour force should achieve long-term benefits from biotechnology. The main types of company involved with biotechnology can be placed in seven categories (Table 1.3).

A key factor in the distinction between biology and biotechnology is their scale of operation. The biologist usually works in the range nanograms to

Table 1.3. *Company categories involved in biotechnology*

Therapeutics	Pharmaceutical products for the cure or control of human diseases including antibiotics, vaccines, gene therapy
Diagnostics	Clinical testing and diagnosis, food, environment, agriculture
Agriculture/forestry/horticulture	Novel crops or animal varieties, pesticides
Food	Wide range of food products, fertilisers, beverages, ingredients
Environment	Waste treatment, bioremediation, energy production
Chemical intermediates	Reagents including enzymes, DNA/RNA, speciality chemicals
Equipment	Hardware, bioreactors, software and consumables supporting biotechnology

milligrams. Biotechnologists working on the production of vaccines may be satisfied with milligram yields, but many other projects aim at kilograms or tonnes. Thus, one of the main aspects of biotechnology consists of scaling-up biological processes.

Many present-day biotechnological processes have their origins in ancient and traditional fermentations such as the brewing of beer and the manufacture of bread, cheese, yoghurt, wine and vinegar. However, it was the discovery of antibiotics in 1929 and their subsequent large-scale production in the 1940s that created the greatest advances in fermentation technology. Since then we have witnessed a phenomenal development in this technology, not only in the production of antibiotics but in many other useful, simple or complex biochemical products, e.g. organic acids, polysaccharides, enzymes, vaccines and hormones (Table 1.4). Inherent in the development of fermentation processes is the growing close relationship between the biochemist, the microbiologist and the chemical engineer. Thus, biotechnology is not a sudden discovery but rather a coming of age of a technology that was initiated several decades ago. Looking to the future, the *Economist*, when reporting on this new technology, stated that it may launch 'an industry as characteristic of the twenty-first century as those based on physics and chemistry have been of the twentieth century'.

Table 1.4. *World markets for biological products, 1981*

Product	Sales ($ millions)
Alcoholic beverages	23 000
Cheese	14 000
Antibiotics	4500
Penicillins	500
Tetracyclines	500
Cephalosporins	450
Diagnostic tests	2000
Immunoassay	400
Monoclonal	5
Seeds	1400
High fructose syrups	800
Amino acids	750
Baker's yeast	540
Steroids	500
Vitamins	
All	330
C	200
B_{12}	14
Citric acid	210
Enzymes	200
Vaccines	150
Human serum albumin	125
Insulin	100
Urokinase	50
Human factor VIII protein	40
Human growth hormone	35
Microbial pesticides	12

If it is accepted that biotechnology has its roots in distant history and has large successful industrial outlets, why then has there been such public awareness of this subject in recent years. Undoubtedly the main dominating reason must derive from the rapid advances in molecular biology, in particular recombinant DNA technology, which is giving human beings dominance over nature. By these new techniques (discussed in Chapters 3, 8 and 10) it is possible to manipulate directly the heritable material (DNA) of cells between different types of organism, creating new combinations of characters and abilities not previously known to be present on this planet. The potential of this series of techniques first developed in academic laboratories is now being rapidly exploited in industry. The industrial benefits are immense but the inherent dangers of tampering with nature must always be appreciated and respected.

While in theory the technology is available to transfer a particular gene from any organism into any other organism, microorganism, plant or animal (Chapter 3), in actual practice there are numerous constraining factors such as which genes are to be cloned, and how they can be selected. The single most limiting factor in the application of genetic engineering is the dearth of basic scientific knowledge of gene structure and function. For plants it is salutary to note that only about 150 plant genes, out of a conservative total of about 10 000, have so far been characterised at the DNA level.

The developments of biotechnology are proceeding at a speed similar to that of microelectronics in the mid-1970s. Although the analogy is tempting, any expectations that biotechnology will develop commercially at the same spectacular rate should be tempered with considerable caution. While the potential of 'new' biotechnology cannot be doubted, a meaningful commercial realisation is now only slowly occurring and will accelerate as we approach the end of the century. New biotechnology will have a considerable impact across all industrial uses of the life sciences. In each case the relative merits of competing means of production will influence the economics of a biotechnological route. Biotechnology will undoubtedly have great benefits in the long term in all sectors.

The growth in awareness of modern biotechnology parallels the serious world-wide changes in the economic climate arising from the escalation of oil prices since 1973. There is a growing realisation that fossil fuels (although, at the time of writing, in a production glut period) and other non-renewable resources will one day be in limited supply. This will result in the requirement of cheaper and more secure energy sources and chemical feedstocks, which biotechnology could perhaps fulfil. Countries with climatic conditions suitable for rapid biomass production could well have major economic advantages over less climatically suitable parts of the world. In particular, the tropics must hold high future potential in this respect.

Another contributory factor to the growing interest in biotechnology has been the current recession in the Western world, in particular the depression of the chemical and engineering sections, in part due to the increased energy costs. Biotechnology has been considered as one important means of restimulating the economy, whether on a local, regional, national or even global basis, using new biotechnological methods and new raw materials. In part, the industrial boom of the 1950s and 1960s was due to cheap oil, whereas the information technology advances in the 1970s and 1980s resulted from developments in microelectronics. It is quite feasible that the 1990s will increasingly be seen as the era of biotechnology. There is undoubtedly a world-wide increase in molecular biological research, the formation of new biotechnological companies, large investments by nations, companies and individuals and the rapid expansion of data bases, information sources and, above all, extensive media coverage.

It is perhaps unfortunate that there has been an over-concentration on the new implications of biotechnology and less identification of the very large traditional biotechnological industrial bases that already function throughout the world and contribute considerably to most nations' gross national products. Indeed, many of the innovations in biotechnology will not appear *a priori* as new products but rather as improvements to organisms and processes in long-established biotechnological industries, e.g. brewing and antibiotics production.

New applications are likely to be seen earliest in the area of healthcare and medicine, followed by that of agriculture and food technology. Exciting new medical treatments and drugs based on biotechnology are appearing with ever-increasing regularity. Prior to 1982 insulin for human diabetics was derived from cow and pig pancreases. The gene for human insulin was then isolated, and cloned into a microorganism, which was then mass-produced by fermentation. This genetically engineered human insulin, identical to the natural human hormone, was the first commercial pharmaceutical product of recombinant DNA technology and now supplies millions of insulin users world wide with a safe, reliable and unlimited source of this vital hormone. Biotechnology has also made it easier to detect and diagnose human, animal and plant diseases. In clinical diagnosis there are now hundreds of specialised kits available for simple home use or for complex laboratory procedures such as blood screening. Biotechnology methods can now improve the nutrition, taste and appearance of plants and various food products, enhance resistance to specific viruses and insect pests and produce safer herbicides. For food safety, new probes can rapidly detect and accurately identify specific microbial pathogens in food, e.g. the bacteria *Salmonella* and *Listeria* and fungal toxins such as aflatoxin.

Applications in chemical production, fuel and energy production, pollution control and resource recovery will possibly take longer to develop and will depend on changes in the relative economics of currently employed technologies. Figure 1.2 shows how the USA is currently applying research and development (R&D) funding to industrial biotechnology.

Biotechnology-based industries will not be labour-intensive and although they will create valuable new employment, the need will be more for brains

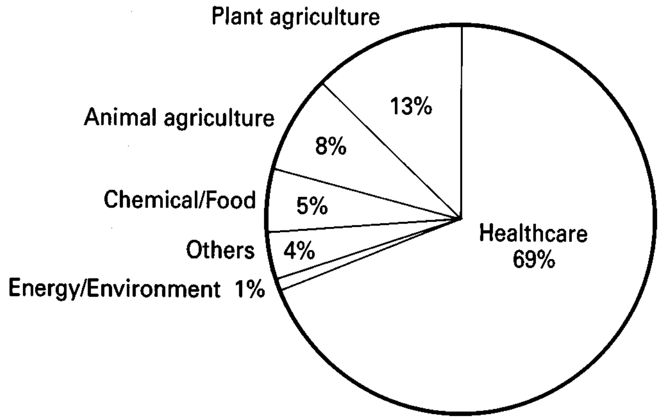

Fig. 1.2 Distribution of research and development funding in industrial biotechnology in the USA.

than muscle. Much of modern biotechnology has been developed and utilised by large companies and corporations. However, many small- and medium-sized companies are realising that biotechnology is not a science of the future but provides real benefits to their industry today. In many industries traditional technology can produce compounds causing environmental damage, whereas biotechnology methods can offer a 'green' alternative promoting a positive public image and also avoiding new environmental penalties. Knowledge of biotechnology innovations must be translated through to all sectors of industry.

Many new, high technology biotechnology companies have arisen from entrepreneurs from academia who are often dominant, charismatic individuals whose primary aim has been to develop a new technology. New biotechnology companies have certain features not often seen in others (Table 1.5). The position of new biotechnology at the interface between academia and industry creates a unique need for abstracting information from a wide range of sources and companies spend large sums on information management.

Biotechnology is high technology *par excellence*. The most exciting and potentially profitable facets of new biotechnology in the next decade will involve R&D at the very frontiers of current knowledge and techniques. In the late 1970s molecular biologists were putting forward vague promises about the wonders of this scientific discipline while the technologies needed to realise it were still being developed and were still requiring immense levels of research and product development funding. Biotechnologists now make predictions with more confidence, since many of the apparently

Table 1.5. *Some unique features of biotechnology companies*

Technology driven and multidisciplinary: product development can involve molecular biologists, clinical researchers, product sales force
Must manage: regulatory authorities, public perception; issues of health and safety; risk assessment
Business climate characterised by rapid change and considerable risk – one biotechnology innovation may quickly supercede another
Biotechnology business growth highly dependent on venture capital – usually needs exceptionally high level of funding before profit sales return

insurmountable problems have been more easily overcome than had been predicted and many transitions from laboratory experiments to large-scale industrial processes have been achieved. Truly, new biotechnology has come of age.

For biotechnology to be commercially successful and exploited there is a need both to recruit a specialist workforce and also for the technology to be understood and applied by practitioners in a wide range of other areas including law, patents, medicine, agriculture, engineering, etc. Higher education will supply the range of specialist disciplines encompassing biotechnology, while some courses will endeavour to produce 'biotechnology' graduates who have covered many of the specialist areas at a less rigorous level than the pure degree specialisation. Also many already employed in biotechnology-based industries must regularly have means of updating or even retraining. To this end, there are now many books on specific aspects of biotechnology together with software programs. The European-based BIOTOL (Biotechnology by Open Learning) has now produced a wide range of learning programs. Such programs are designed not only for the needs of students but also for company training activities and are written in a user-friendly style of good, open learning materials. The currency of biotechnology throughout the world will be an educated, skilled workforce and ready access to the ever-widening knowledge and resource base. Science has defined the world in which we live, and biotechnology, in particular, will become an essential and accepted activity of our culture.

1.3 Biotechnology – a three-component central core

Many biotechnological processes may be considered as having a three-component central core, in which one part is concerned with obtaining the best biological catalyst for a specific function or process, the second part creates (by construction and technical operation), the best possible environment for the catalyst to perform, and the third part (downstream processing) is concerned with the separation and purification of an essential product or products from a fermentation process.

In the majority of examples so far developed, the most effective, stable and convenient form for the catalyst for a biotechnological process is a whole organism and it is for this reason that so much of biotechnology revolves around microbial processes. This does not exclude the use of higher organisms; in particular, plant and animal cell culture will play an increasingly important role in biotechnology.

Microorganisms can be viewed both as primary fixers of photosynthetic energy and as systems for bringing about chemical changes in almost all types of natural and synthetic organic molecules. Collectively, they have an immense gene pool that offers almost unlimited synthetic and degradative potential. Furthermore, microorganisms can possess extremely rapid growth rates far in excess of any of the higher organisms such as plants and animals. Thus, immense quantities can be produced under the right environmental conditions in short time periods.

The methodologies that are in general use enable the selection of improved microorganisms from the natural environmental pool, the modification of microorganisms by mutation and, more recently, the mobilisation of a spectacular array of new techniques, deriving from molecular biology, which may eventually permit the construction of microorganisms, plants and animals with totally novel biochemical potentials (Chapter 3). These new techniques have arisen largely from fundamental achievements in molecular biology over the last two decades.

These manipulated and improved organisms must be maintained in substantially unchanged form and this involves another spectrum of techniques for the preservation of organisms, for retaining essential features during industrial processes and, above all, retaining long-term vigour and viability. In many examples the catalyst is used in a separated and purified form, namely as enzymes, and a huge amount of information has been built up on the large-scale production, isolation and purification of individual enzymes and on their stabilisation by artificial means (Chapter 5).

The second part of the core of biotechnology encompasses all aspects of the containment system or bioreactor within which the catalysts must function (Chapter 4). Here the combined specialist knowledge of the bioscientist and bioprocess engineer will interact, providing the design and instrumentation for the maintenance and control of the physicochemical environment such as temperature, aeration, pH, etc., thus allowing the optimum expression of the biological properties of the catalyst. Having achieved the required end-point of the biotechnological process within the bioreactor, e.g. biomass or biochemical product, in most cases it will be necessary to separate the organic products from the predominantly aqueous environment. This third aspect of biotechnology, namely downstream processing, can be a technically difficult and expensive procedure, and is the least understood area of biotechnology. Downstream processing is primarily concerned with initial separation of the bioreactor broth or medium into a liquid phase and a solids phase, and subsequent concentration and purification of the product. Processing will usually involve more than one stage. Downstream processing costs (as approximate proportions of selling prices) of fermentation products, vary considerably, e.g. with yeast biomass, penicillin G and certain enzymes processing costs as percentages of selling price are 20%, 20–30% and 60–70%, respectively.

Successful involvement in a biotechnological process must draw heavily upon more than one of the input disciplines. The main areas of application of biotechnology are shown in Table 1.6 while Fig. 1.3 attempts to show the input of many disciplines into the biotechnological processes together with the differing enabling technologies.

Biotechnology will continue to create exciting new opportunities for commercial development and profits in a wide range of industrial sectors including, healthcare and medicine, agriculture and forestry, fine and bulk chemicals production, food technology, fuel and energy production, pollution control and resource recovery. Biotechnology offers a great deal of hope for solving many of the problems our world faces!

1.4 Product safety

In biotechnology, governmental regulations will represent a critical determinant on the time and total costs in bringing a product to market. Regulatory agencies can act as 'gate-keepers' for the development and availability of new biotechnology products and may erect considerable barriers to industrial development. In practice, such barriers come from the costs of testing products to meet regulatory standards, possible delays and uncertainties in regulatory approval and even outright disapproval of new products on grounds of safety. The very considerable costs that may be required to ensure product safety can often discourage new research or curtail product development if a future new product is not likely to have a high financial market return. Concern has been expressed in the USA that overzealous and perhaps

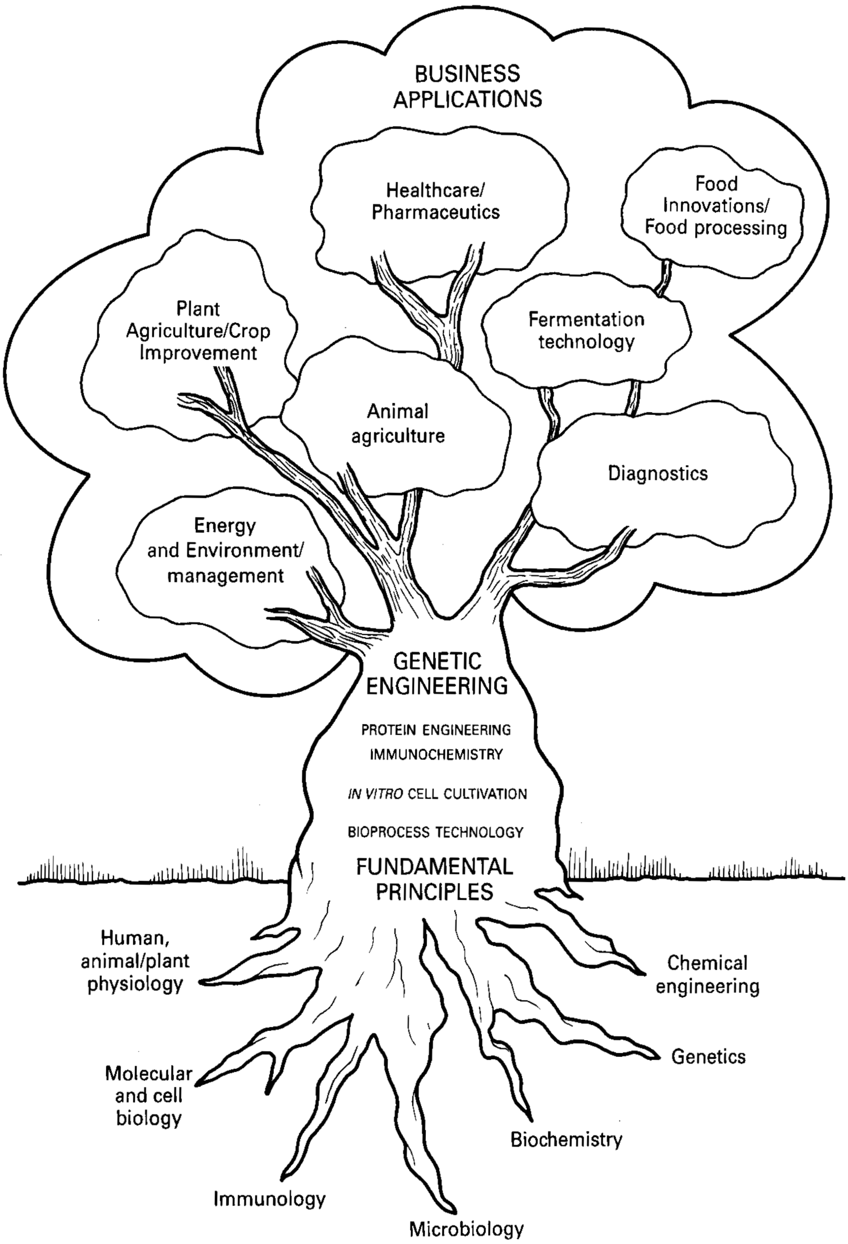

Fig. 1.3 The biotechnology tree.

Table 1.6. *The main areas of application of biotechnology*

Bioprocess technology Historically, the most important area of biotechnology, namely brewing, antibiotics, mammalian cell culture, etc.; extensive development in progress with new products envisaged, namely polysaccharides, medically important drugs, solvents, protein-enhanced foods. Novel fermenter designs to optimise productivity
Enzyme technology Used for the catalysis of extremely specific chemical reactions; immobilisation of enzymes; to create specific molecular converters (bioreactors). Products formed include L-amino acids, high fructose syrup, semi-synthetic penicillins, starch and cellulose hydrolysis, etc. Enzyme probes for bioassays
Waste technology Long historical importance but more emphasis now being made to couple these processes with the conservation and recycling of resources; foods and fertilisers, biological fuels
Environmental technology Great scope exists for the application of biotechnological concepts for solving many environmental problems – pollution control, removing toxic wastes; recovery of metals from mining wastes and low-grade ores
Renewable resources technology The use of renewable energy sources, in particular, lignocellulose to generate new sources of chemical raw materials and energy ethanol, methane and hydrogen. Total utilisation of plant and animal material
Plant and animal agriculture Genetically engineered plants to improve nutrition, disease resistance, keeping quality, improved yields and stress tolerance will become increasingly commercially available. Improved productivity, etc., for animal farming. Improved food quality, flavour, taste and microbial safety
Healthcare New drugs and better treatment for delivering medicines to diseased parts. Improved disease diagnosis, understanding of the human genome

unrealistic regulatory requirements are damaging the future industrial development of some areas of biotechnology and, consequently, are systematically de-escalating their regulatory requirements. The use of recombinant DNA technology has created the greatest areas of possible safety concern (Chapters 13 and 14). Public attitudes to biotechnology are most often related to matters of perceived or imaginary dangers in the techniques of genetic manipulation.

1.5 Public perception of biotechnology

While biotechnology presents enormous potential for healthcare and the production, processing and quality of foods by genetic engineering of crops, fertilisers, pesticides, vaccines and various animal and fish species, the implications of these new biotechnological processes go well beyond the technical benefits offered. The implementation of the new techniques will be dependent upon their acceptance by consumers (Chapter 14). As stated in the Advisory Committee on Science and Technology report *Developments in Biotechnology* 'Public perception of biotechnology will have a major influence on the rate and direction of developments and there is growing concern about genetically modified products. Associated with genetic manipulation are diverse questions of safety, ethics and welfare.'

Public debate is essential for new biotechnology to grow up and, undoubtedly for the foreseeable future, biotechnology will be under scrutiny. Public understanding of these new technologies could well hasten public acceptance. However, the low level of scientific literacy (e.g. in the USA, where only 7% of the population are scientifically literate) does mean that most people will not be able to draw informed conclusions about this important biotechnology issue. Consequently, it is conceivable (and indeed occurring) that a small number of activists can argue the case against genetic engineering in such emotive and ill-reasoned ways that the public and the politicians are misled. The biotechnology community needs to sit up and take notice of, and work with, the public. People influence decision-making by governments through the ballot box or through the presence of public opinion. Ultimately the benefits of biotechnology will speak for themselves as will be seen in the following chapters.

1.6 Biotechnology and the developing world

Successful agriculture holds the answer to the poverty gap between the rich and poor nations. In the developed world, agricultural sciences are well developed, producing an abundance of high quality products. Agricultural biotechnology (Chapter 10) will further improve quality, variety and yield. Will these new plant species, improved by genetic engineering, find their way to the developing countries, ensuring higher productivity, greater resistance to disease and be more marketable? It is not yet clear what will happen other than that the affluent nations will become increasingly well endowed with an abundance of food. World-wide there will be enough food for all but will it always continue to be disproportionately distributed? Biotechnology developments need high inputs of finance and skilled workforces – both of which are in short supply in most developing nations.

While many developing nations have successfully collaborated in the past with Western biotechnology companies, it is salutary to note that between 1986 and 1991 the percentage of arrangements implemented by US biotechnology companies with developing countries dropped from 20% to 3%! The ability of developing nations to avail themselves of the many promises of new biotechnology will to a large extent depend on their capacity to integrate modern developments of biotechnology within their own research and innovation systems, in accordance with their own needs and priorities.

In the following chapters some of the most important areas of biotechnology are considered with a view to achieving a broad overall understanding of the existing achievements and future aims of this new area of technology. However, it must be appreciated that biotechnological development not only will depend on scientific and technological advances, but will also be subject to considerable political, economic and, above all, public acceptance. Finally, it has been said that most scientific disciplines pass through golden ages when new approaches open the door to rapid and fundamental expansion. Biotechnology is just now entering this golden period. A spectacular future lies ahead.